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# Short and Long Term Effects of Psychosocial Factors on the Outcome of Coronary Artery Bypass Surgery

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Zsuzsanna Cserép, Andrea Székely and Bela Merkely

Additional information is available at the end of the chapter

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## 1. Introduction

Coronary heart disease (CHD) is the commonest form of heart disease in the developed world, and one of the leading causes of mortality and morbidity in these countries. Over the past decades numerous studies focused on the link between CHD and different psychosocial factors. The prevalence of depression in patients with diagnosed CHD is quoted between 20 and 45%. Elevated anxiety scores have been reported for 20 to 55% [1]. Emotional factors and the experience of chronic stress contribute to the development of atherosclerosis and cardiac events. Emotional factors include affective disorders such as major depression and anxiety disorders as well as hostility and anger. Chronic stressors include factors such as low social support and low socioeconomic status [2]. Similar prevalence ratios have been found for patients undergoing coronary artery bypass graft surgery (CABG). Symptoms of anxiety and unipolar depression are common psychological disturbances among patients undergoing CABG surgery. Numerous prospective cohort studies focus on the short and long term outcome of CABG. Research revealed that not only clinical factors e.g. cardiac status, comorbidities and intraoperative factors have impact on the outcome [3]. Comparison of morbidity and mortality rates associated with psychosocial factors to morbidity and mortality rates related to traditional risk factors (smoking, obesity, and physical inactivity) showed priority of psychosocial background [4].

The purpose of this review is to provide a selected summary of key findings in this literature. We summarize some of the classic studies and historical developments important to the field and focus on prospective data on cardiac surgery patients. We review the literature on the important psychosocial domains (depression, anxiety, self rated health, happiness, illness intrusiveness, quality of life, gender differences, social support, negative affectivity, social inhibition, education) that have received much of the research attention, discuss key patho-

physiological mechanisms and pathways by which psychosocial factors may influence the outcome after surgery, and discuss some treatment directions likely to be critical to advancing the field.

## 2. Depression

### 2.1. Depression and Coronary Heart Disease (CHD)

Among emotional factors, depression has been most widely studied in recent years. Depressive disorders vary from mild (subclinical) depressive symptoms to classic major depression. According to the Diagnostic and Statistical Manual of Mental Disorders, depression is characterized by low mood and/or anhedonia (lose interest in activities that once were pleasurable) that lasts for two weeks or more and is accompanied by significant functional impairment and somatic complaints (insomnia, excessive sleeping, fatigue, loss of energy, or aches, pains or digestive problems that are resistant to treatment) [2]. Depression is 3 times more common in patients after an acute myocardial infarction than in the general community. In-hospital prevalence of major depression was 15% to 20% of patients with myocardial infarction, and an even more patients showed an elevated level of depressive symptoms [5]. Depression is regarded as an independent risk factor for atherosclerotic deposits in coronary arteries. The pathophysiological background covers hypercortisolaemia related to e.g. insulin resistance, sympathetic vagal dysbalance related to e.g. disturbed regulation of blood pressure, reduced heart rate variability, hypothalamic-pituitary-adrenal axis dysfunction, increased plasma platelet factor 4 (suggesting enhanced platelet activation), impaired vascular function, and increased C-reactive protein and fibrinogen levels (suggesting increased inflammatory response) and an unfavourable lifestyle like cigarette smoking, unhealthy diet, and lack of physical activity, medication adherence, as well as social isolation and chronic life stress [1, 5]. Depressive patients have higher risk of non-compliance with medical treatment regimens, therefore reduced chances of successful modifications of other cardiac risk factors and participation in cardiac rehabilitation, and have greatly reduced quality of life [5]. Major depression and elevated depressive symptoms are associated with worse prognosis in patients with CHD: in the Prospective Epidemiological Study of Myocardial Infarction (PRIME) Study, a multicenter, observational, prospective cohort, in healthy, European, middle-aged men were surveyed for the occurrence of first coronary heart disease and stroke events over 10 years. At baseline a questionnaire was used to define the presence of depressive symptoms. Results suggested that, baseline depressive symptoms are associated with an increased risk of coronary heart disease in the short-term and for stroke in the long-term [6]. Barefoot et al. assessed 1250 patients with documented CHD using the Zung Self-Report Depression Scale at the time of diagnostic coronary angiography and followed patients for up to 19.4 years. Results showed that patients with moderate to severe depression were at 69% greater risk for cardiac death and 78% greater risk for all-cause death [7]. Frasure-Smith et al. assessed gender differences in the impact of depression on 1-year cardiac mortality in patients hospitalized for an acute myocardial infarction. Increased depression scores were

significantly related to cardiac mortality for both genders (the odds ratio for women was 3.29, for men, the odds ratio was 3.05). Data were controlled for other multivariate predictors of mortality (age, Killip class, the interactions of gender by non-Q wave myocardial infarction, gender by left ventricular ejection fraction, and gender by smoking) and showed that depression was independent predictor for either gender [8]. Most studies that have examined the relationship between increasing depression severity and cardiac events have shown a dose-response relationship: in a 5-year-follow-up study post-myocardial infarction patients were recruited and assigned to categories based on the severity of depressive symptoms, ranging from no depressive symptoms to moderate to severe depressive symptoms. During follow-up period, a gradient relationship was observed between the magnitude of depressive symptoms and the frequency of deaths, with increased events occurring even in patients with mild depressive symptoms [9]. In the prospective study of Brown et al. elderly adults with significant depressive symptoms at baseline and without a current diagnosis of CHD at baseline were more likely to experience a cardiac event over a 15-year follow-up period. Depressed patients were 1.5 times more likely to suffer a cardiac event (i.e., acute myocardial infarction or cardiac death), even after controlling for demographics and known cardiovascular risk factors. The elevated depressive symptom severity is a predictor of cardiac events among older women and men as well as older white and black adults [10]. Despite methodological differences (sample sizes, sample characteristics, selection of covariates, etc) from study to study, the data from prospective studies with objective outcome measures and validated questionnaires for depression are remarkably consistent in their results suggesting depression is a risk factor for both the development of and the worsening of CHD [5].

## 2.2. Depression and CABG

CABG surgery is a common surgical intervention for CHD patients and prevalence of depression before or after CABG surgery is about 20–25% [4]. The presence of elevated levels of depressive symptoms results in a higher risk of mortality and significantly increased overall risk of major cardiac events following cardiac surgery [11]. In the prospective study of Connerney et al. 309 CABG patients were followed for 1 year after surgery. Compared with non depressed patients, depressed patients were more than twice as likely to have a cardiac event within 12 months after surgery but were not at higher risk for mortality within the first year [4]. In a larger sample of 817 CABG patients followed for up to 12 years, Blumenthal et al. assessed the effect of depression on mortality after CABG surgery. Depression was assessed both at baseline and 6 months after surgery. Results indicated that moderate to severe depression on the day before surgery as well as depression that persisted from baseline to 6 months after surgery were associated with 2-fold to 3-fold increased risk of mortality after adjustment for other risk factors [3]. Readmission following cardiac surgery is a significant burden on the healthcare system. In a prospective study, 226 CABG patients completed baseline self-report measures of depression, anxiety and stress and 222 patients completed these measures after surgery on the hospital ward. In multivariable analyses more than two-fold increase in readmission risk was associated with preoperative anxiety and postoperative depression, independent of covariates [12]. When our work group investigated the relation-

ship between depression, anxiety, education, social isolation and mortality 7.5 years after cardiac surgery, we found that there was a significant difference in depression (measured with Beck Depression Inventory (BDI)) between survivors and non survivors preoperatively, after discharge and in both intervals (Figure 1) [13].

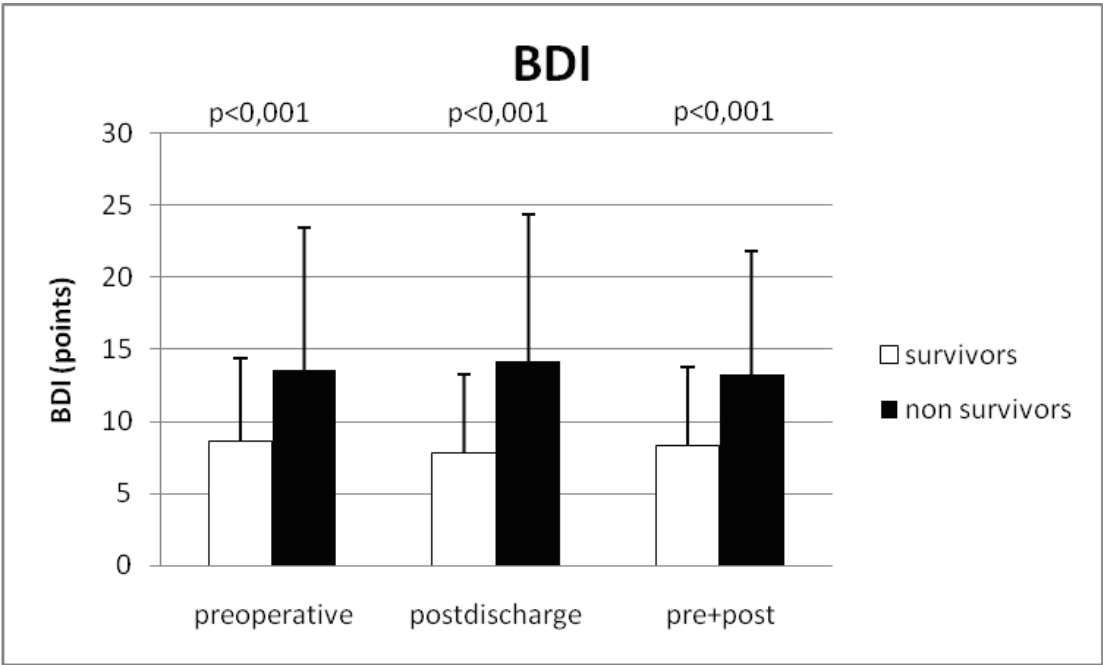
First author and title	Number of patients	Methods	Results
Blumenthal JA. Depression as a risk factor for mortality after coronary artery bypass surgery.	817	CABG patients completed the Center for Epidemiological Studies-Depression (CES-D) scale before surgery, 6 months after CABG, and were followed-up for up to 12 years.	Patients with moderate to severe depression at baseline (adjusted hazard ratio [HR] 2.4, [95% CI 1.4-4.0]; p=0.001) and mild or moderate to severe depression that persisted from baseline to 6 months (adjusted HR 2.2, [1.2-4.2]; p=0.015) had higher rates of death than did those with no depression.
Connerney I. Relation between depression after coronary artery bypass surgery and 12-month outcome: a prospective study.	207 men and 102 women	CABG patients screened for depression with a structured psychiatric interview (diagnostic interview schedule) and a questionnaire (Beck depression inventory) before discharge. Outcome: cardiac events included angina or heart failure that needed admission to hospital, myocardial infarction, cardiac arrest, percutaneous transluminal coronary angioplasty, repeat CABG, and cardiac mortality. Non-cardiac events consisted of all other reasons for mortality or readmission.	63 patients (20%) met criteria for major depressive disorder. At 12 months, 17 (27%) of these patients had a cardiac event compared with 25 of 246 (10%) who were not depressed (p<0.0008). In a Cox proportional-hazard model with these five and two other variables of cardiac severity, major depressive disorder (risk ratio 2.3 [95% CI 1.17-4.56]), low ejection fraction (2.3 [1.07-5.03]), and female sex (2.4 [1.24-4.44]) were associated with adverse outcomes. Depression did not predict deaths or admissions for non-cardiac events.
Majed B. Depressive symptoms, a time-dependent risk factor for coronary heart disease and stroke in middle-aged men: the PRIME Study.	9601 men	The occurrence of first coronary heart disease (n=647) and stroke events (n=136) over 10 years among healthy men.	Depressive symptoms at baseline were associated with coronary heart disease in the first 5 years of follow-up (hazard ratio, 1.43; 1.10-1.87) and with stroke in the second 5 years of follow up (hazard ratio, 1.96; 1.21-3.19) after adjustment. The association was even stronger for ischemic stroke (n=108; hazard ratio, 2.48; 1.45-4.25).
Barefoot JC. Depression and long-term mortality risk in patients with coronary artery disease.	1250	Patients with established CAD were assessed for depression with the Zung Self-Rating Depression Scale and followed for subsequent mortality. Follow-up ranged up to 19.4 years.	Depression was associated with increased risk of cardiac death (p = 0.002) and total mortality (p < 0.001) after controlling for initial disease severity and treatment. Patients with moderate to severe depression had a 69% greater odds of cardiac death and a 78% greater odds of mortality from all causes than nondepressed patients. Patients with moderate to severe

			depression had an 84% greater risk 5 to 10 years later and a 72% greater risk after "> 10 years compared with the nondepressed.
Frasure-Smith N. Gender, depression, and one-year prognosis after myocardial infarction.	613 men 283 women	Beck Depression Inventory (BDI) was used to assess depression symptoms during hospitalization after an acute myocardial infarction.	There were 290 patients (133 women) with at least mild to moderate symptoms of depression; 8.3% of the depressed women died of cardiac causes in contrast to 2.7% of the nondepressed. For depressed men, the rate of cardiac death was 7.0% in contrast to 2.4% of the nondepressed. Increased BDI scores were significantly related to cardiac mortality for both genders [the odds ratio for women was 3.29 (95% confidence interval (CI) = 1.02-10.59); for men, the odds ratio was 3.05 (95% CI = 1.29-7.17)]. Control for other multivariate predictors of mortality in the data set (age, Killip class, the interactions of gender by non-Q wave MI, gender by left ventricular ejection fraction, and gender by smoking) did not change the impact of the BDI for either gender.
Lesperance F. Five-year risk of cardiac mortality in relation to initial severity and one-year changes in depression symptoms after myocardial infarction	896	Beck Depression Inventory was administered to the patients after myocardial infarction during admission and at 1 year. Five-year survival was ascertained using Medicare data	Significant long-term dose-response relationship between depression symptoms during hospitalization and cardiac mortality was observed. Results remained significant after control for multiple measures of cardiac disease severity. Although 1-year scores were also linked to cardiac mortality, most of that impact was explained by baseline scores. Improvement in depression symptoms was associated with less cardiac mortality only for patients with mild depression. Patients with higher initial scores had worse long-term prognosis regardless of symptom changes.
Brown JM. Risk of coronary heart disease events over 15 years among older adults with depressive symptoms	2728	Depressive symptom severity at baseline was assessed by the Center for Epidemiologic Studies Depression Scale among primary care practice patients. Data regarding baseline demographic and clinical variables, as well as laboratory evidence of acute MI, were obtained from an electronic medical record system. All-cause mortality and CHD death were determined from the National Death Index through 2006.	Cox proportional hazards models showed that individuals with elevated depressive symptoms were more likely to experience a CHD event, even after adjustment for demographics and comorbid health conditions (relative risk = 1.46, 95% confidence interval: 1.20-1.77). Depression status was also a significant predictor of all-cause mortality in adjusted models.



Tully PJ. The role of depression and anxiety symptoms in hospital readmissions after cardiac surgery.	226	Hospital readmissions after coronary artery bypass graft surgery were assessed.	When analyzed as continuous variables in multivariable analyses, preoperative anxiety and postoperative depression predicted readmissions independent of medical covariates. In multivariable analyses with dichotomized anxiety, depression and stress, more than two-fold increase in readmission risk was attributable to preoperative anxiety and postoperative depression, independent of covariates.
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**Table 1.** Some important studies about depression and CABG



**Figure 1.** Figure shows significant difference in depression (BDI points) between survivors and non survivors preoperatively, after discharge and in both intervals.

### 3. Anxiety

#### 3.1. Anxiety and coronary heart disease

Anxiety has been characterized as a future-oriented, negative affective state with a component of fear, resulting from the perception of threat and the individual’s perceived inability to predict, control, or obtain the desired results in upcoming situations. Somatic manifestations are tachycardia, hyperventilation, sweating, psychological manifestations are feelings of apprehension, nervousness, restlessness, and may also cause changes in sleeping pattern [13].

Pathophysiological background by which anxiety influences outcome in ischemic heart disease is largely unknown. An increased incidence of ECG QT interval prolongation has been demonstrated among patients with anxiety, which increases the occurrence of ventricular arrhythmia [14]. Patients with anxiety have been shown consistently to have sympathetic nervous system upregulation, with excessive catecholamine production [15]. Furthermore, impaired vagal control, manifest as an impaired baroreflex response and a decrease in heart rate variability has been noted in patients with anxiety. Impairment of the baroreflex response and decreased heart rate variability are each thought to be sensitive markers for abnormalities in autonomic cardiovascular regulation and are independent risk factors for sudden cardiac death [16, 17, 18]. Patients with anxiety and CAD often show an exaggerated systemic response to stress, characterized by an abnormally increased production of catecholamines, which can result in increased myocardial oxygen demand due to elevations in heart rate, blood pressure, and the rate of ventricular contraction [19]. In addition to the biological risks of anxiety, the additive effects of adverse behavioural risk factors (e.g., excessive nicotine and perhaps caffeine) in anxious patients have also be taken into account [20]. Anxiety is very common in patients with myocardial infarction, with an in-hospital occurrence rate of 30% to 40% [21]. Studies with coronary patients suggest that anxiety disorders may be associated with greater mortality, particularly sudden cardiac death, and greater cardiovascular morbidity. Higher levels of anxiety have been associated with poorer prognosis and greater recurrence of cardiac events after myocardial infarction [22]. In a cohort study the relative importance of depression, anxiety, anger, and social support in predicting 5-year cardiac-related mortality following a myocardial infarction was investigated. Higher level of anxiety predicted greater cardiac-related mortality in a sample of nearly 900 patients with myocardial infarction, but this effect was non significant following adjustment for disease severity [23]. The first meta-analysis on the association of anxiety and coronary heart disease showed a consistent association between anxiety and impaired prognosis after myocardial infarction, with a 36% increased risk for mortality (cardiac and all-cause) and for cardiac events. Limitation of the result was the pooled odds ratios for cardiac death, because it was based on only four studies [21].

### **3.2. Anxiety and CABG**

Anxiety is especially high for CABG patients while they are on the waiting list with an unknown surgery date [24]. The patients have fear of dying before, rather than during surgery, and this fear influenced strongly their level of anxiety. Anxiety also manifests as an activator of sympathetic and parasympathetic nervous systems and cardiovascular excitation that can exacerbate CAD symptoms. After surgery, while anxiety may decrease to below pre-operative level, the severity of anxiety does not necessarily remit to below sub-clinical levels and may warrant intervention [25]. In the Post-CABG Trial the presence of anxiety symptoms was significantly associated with a higher incidence rate of death or myocardial infarction after a median follow-up time of 4.3 years following CABG. After controlling for the presence of depressive symptoms and other covariates (age, gender, race, treatment assignment and years since CABG surgery), a significant dose-response relationship persisted between anxiety and mortality. The observed dose-response relationship between level of anxiety and risk of death or myocardial infarction underlines the importance of even lower levels of anxiety. The risk



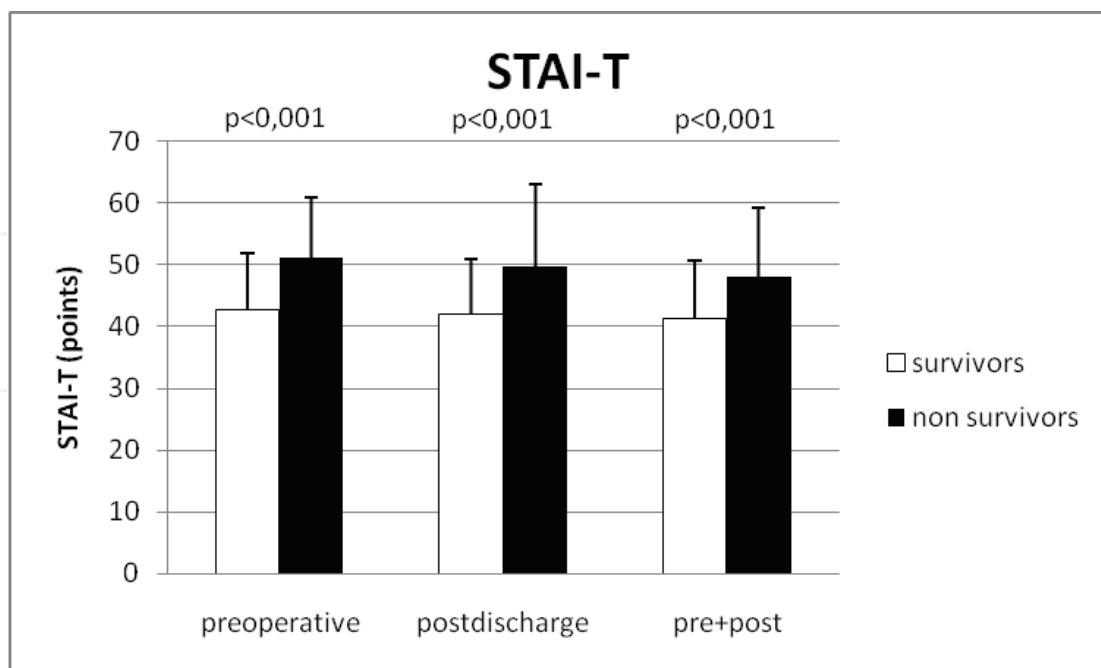
of death or myocardial infarction in those with both depressive and anxiety symptoms was what would be expected from the combination of the independent effects [26]. In a study of our workgroup trait anxiety was associated with increased mortality and cardiovascular morbidity. In our population trait anxiety remained an independent predictor for post-discharge cardiovascular events and 4 year mortality. Moreover, post-discharge 6th month trait anxiety scores were more predictive for cardiovascular events compared to the preoperative values. Although anxiety and depression were positively and highly correlated in these patients, only anxiety was associated with increased mortality and morbidity. In addition trait anxiety was significantly higher in patients hospitalized with arrhythmia, congestive heart failure or myocardial infarction during a 4 year period after cardiac (CABG and valve) surgery [27]. In another study of our workgroup depression, anxiety, education, social isolation and mortality together were investigated 7.5 years after cardiac surgery. Our results have suggested that the assessment of psychosocial factors, particularly anxiety and education may help identify patients at an increased risk for long-term mortality after cardiac surgery (Figure 2.) [13]. Anxiety was also reported to be associated with twofold risk for fatal CHD and more than fourfold risk for sudden death [28]. In a retrospective study 17,885 discharge records of patients after primary CABG surgery were identified. In the sample of rural patients the prevalence of anxiety disorder was 27%. Anxiety was a significant independent predictor of both length of hospital stay and non routine discharge [29]. In a prospective study on cardiac-related readmission within 6 months of CABG postoperative anxiety was identified as both a univariate risk factor and a multivariate risk factor for CHD and surgery-related readmission both with and without adjustment for covariates [30].

First author and title	Number of patients	Methods	Results
Cserep Z. The impact of preoperative anxiety and education level on long-term mortality after cardiac surgery.	180	Anxiety (Spielberger State-Trait Anxiety Inventory, STAI-S/STAI-T), depression (Beck Depression Inventory, BDI) and the number and reason for rehospitalizations were assessed each year in cardiac surgery patients.	During a median follow-up of 7.6 years (25th to 75th percentile, 7.4 to 8.1 years), the mortality rate was 23.6% (95% confidence interval [CI] 17.3-29.9; 42 deaths). In a Cox regression model, the risk factors associated with an increased risk of mortality were a higher EUROSCORE (points; Adjusted Hazard Ratio (AHR):1.30, 95%CI:1.07-1.58)), a higher preoperative STAI-T score (points; AHR:1.06, 95%CI 1.02-1.09), lower education level (school years; AHR:0.86, 95%CI:0.74-0.98), and the occurrence of major adverse cardiac and cerebral events during follow up (AHR:7.24, 95%CI: 2.65-19.7). In the postdischarge model, the same risk factors remained.

Frasure-Smith N. Depression and other psychological risks following myocardial infarction	896	Beck Depression Inventory, state scale of the State-Trait Anxiety Inventory, 20-item version of the General Health Questionnaire, Modified Somatic Perception Questionnaire, Anger Expression Scale, Perceived Social Support Scale, number of close friends and relatives, and visual analog scales of anger and stress were assessed to predict 5-year cardiac-related mortality following a myocardial infarction.	The Beck Depression Inventory ( $P<0.001$ ), the State-Trait Anxiety Inventory ( $P=0.04$ ), and the 20-item version of the General Health Questionnaire ( $P=0.048$ ) were related to outcome, but only depression remained significant after adjustment for cardiac disease severity (hazards ratio per SD, 1.46; 95% confidence interval, 1.18-1.79) ( $P<0.001$ ). There was also a covariate-adjusted trend between negative affectivity scores and outcome ( $P=0.08$ ). Furthermore, residual depression scores ( $P=0.001$ ) and negative affectivity scores ( $P=0.05$ ) were linked to cardiac-related mortality after adjustment for each other and cardiac covariates.
Koivula M. Fear and anxiety in patients at different time-points in the coronary artery bypass process.	171	CABG patients completed questionnaires while awaiting surgery at home, in hospital the evening before surgery and 3 months later. The Bypass Grafting Fear scale was developed to measure fear. Anxiety was measured using State-Trait-Anxiety Inventory.	The highest levels of fear and anxiety were measured in the waiting period to coronary CABG. Compared with the waiting period, fear and anxiety levels dropped in hospital and 3 months later. Female gender was related to change in fear and anxiety.
Rosenbloom JI. Self-reported anxiety and the risk of clinical events and atherosclerotic progression among patients with Coronary Artery Bypass Grafts (CABG).	1317	CABG patients were randomized to either aggressive or moderate lipid lowering and to either warfarin or placebo. Patients were followed up for clinical end points and coronary angiography was conducted at enrollment and after a median follow-up of 4.3 years. Anxiety symptoms were assessed at enrollment using the state portion of the Spielberger State-Trait Anxiety Inventory (STAI)	STAI score $\geq 40$ was positively associated with risk of death or myocardial infarction (MI) (OR 1.55, 95% CI 1.01-2.36, $P=0.044$ ). This association was attenuated slightly when depressive symptoms were included in the model, but lost statistical significance ( $P=0.11$ ). There was a dose-response relationship between STAI score and risk of death or myocardial infarction. There was no association between self-reported anxiety and atherosclerotic progression of grafts.
Székely A. Anxiety predicts mortality and morbidity after coronary artery and valve surgery--a 4-year follow-up study.	180	Patients who underwent cardiac surgery using cardiopulmonary bypass were prospectively studied and followed up for 4 years. Anxiety (Spielberger State-Trait Anxiety Inventory, STAI-S/STAI-T), depression (Beck Depression Inventory, BDI), living alone, and education level along with clinical risk factors and	Average preoperative STAI-T score was $44.6 \pm 10$ . Kaplan-Meier analysis showed a significant effect of preoperative STAI-T $\geq 45$ points ( $p=0.008$ ) on mortality. In multivariate models, postoperative congestive heart failure (OR: 10.8; 95% confidence interval [CI]: 2.9-40.1; $p=0.009$ ) and preoperative

		perioperative characteristics were assessed. Psychological self-report questionnaires were completed preoperatively and 6, 12, 24, 36, and 48 months after discharge. Clinical end-points were mortality and cardiac events requiring hospitalization during follow-up.	STAI-T (score OR: 1.07; 95% CI: 1.01-1.15; p = 0.05) were independently associated with mortality. The occurrence of cardiovascular hospitalization was independently associated with postoperative intensive care unit days (OR: 1.41; 95% CI: 1.01-1.96; p =0.045) and post discharge 6th month STAI-T (OR: 1.06; 95% CI:1.01-1.13; p = .03).
Kawachi I. Symptoms of anxiety and risk of coronary heart disease. The Normative Aging Study.	402 cases of incident coronary heart disease	An anxiety symptoms scale was constructed out of five items from the Cornell Medical Index, which was administered to the cohort at baseline. During 32 years of follow-up incidence of CHD was observed.	Compared with men reporting no symptoms of anxiety, men reporting two or more anxiety symptoms had elevated risks of fatal CHD (age-adjusted odds ratio [OR] = 3.20, 95% confidence interval [CI]: 1.27 to 8.09), and sudden death (age-adjusted OR = 5.73, 95% CI: 1.26 to 26.1). The multivariate OR after adjusting for a range of potential confounding variables was 1.94 (95% CI: 0.70-5.41) for fatal CHD and 4.46 (95% CI: 0.92-21.6) for sudden death. No excess risks were found for nonfatal myocardial infarction or angina.
Dao TK. Gender as a moderator between having an anxiety disorder diagnosis and coronary artery bypass grafting surgery (CABG) outcomes in rural patients.	17,885	Patients who underwent a primary CABG surgery were identified. Independent variables included age, gender, race, median household income based on patient's ZIP code, primary expected payer, the Deyo, Cherkin, and Ciol Comorbidity Index, and an anxiety comorbidity diagnosis. Outcome variables included in-hospital length of stay and patient disposition (routine and nonroutine discharge).	27% of rural patients had a comorbid anxiety diagnosis. Rural patients who had nonroutine discharge were more likely to have comorbid anxiety diagnosis compared to rural patients who had a routine discharge. There was a significant interaction effect between having an anxiety diagnosis and gender on length of hospital stay but not for patient disposition.
Oxlad M. Psychological risk factors for cardiac-related hospital readmission within 6 months of coronary artery bypass graft surgery.	119	Consecutive patients awaiting elective CABG, completed a battery of psychosocial measures in a three-stage repeated-measures design. Relevant medical data were also extracted from patients' medical records 6 months postoperatively to allow for the examination of potential covariates.	Increased postoperative anxiety and increased preoperative depression, were identified as risk factors for cardiac-related readmission independent of the only significant covariate identified, cardiopulmonary bypass time.

**Table 2.** Some important studies about anxiety and CABG



**Figure 2.** Figure shows significant difference in STAI-T (State-Trait Anxiety Inventory) between survivors and non survivors preoperatively, after discharge and in both intervals.

#### 4. Self rated health

Self-rated health (SRH) is measured with a simple question "How do you rate your health in general?" There are five possible responses: very good, good, fair, poor and very poor [31]. Self rated health has been shown to be a potent predictor of mortality and morbidity, functional decline, disability and utilization of health care even after controlling for several sociodemographic and health indicators. The association can be explained by three ways: (1) SRH is a more comprehensive and sensitive measure of health status than the other psychosocial covariates in the analyses; (2) SRH measures individual optimistic or pessimistic disposition, that as such, may be associated with survival; or (3) SRH also measures characteristics other than health status itself, such as family history, health behaviour, and social and psychological resources [32]. In a review SRH was described as an active cognitive process that is independent from formal definitions of health. Self rated health covers bodily sensations that are directly available only to the individuals. These sensations may reflect important physiological dysregulations, such as inflammatory processes. SRH is an individual and subjective conception that is related to death, and builds a connection from the social world and psychological to the biological world. Therefore the answer to the SRH question may summarize the dimensions of health that are most important and determinant to each individual [33]. SRH has been described as one of the most important health outcomes available and recommended as a tool for disease risk screening, as an outcome indicator in the primary care, and standard part of clinical trials [34]. Several studies in different field confirmed the importance of SRH, one of them described that good self health 3 months after PCI predicted good clinical outcome

after 4 years [35]. SRH was reported as an independent predictor of long term mortality in older women after myocardial infarction. Patients dissatisfied with their general health status were at more than six times higher risk of mortality than the satisfied ones [36]. There are only few data available on the link between CABG and SRH. Oxlad et al. investigated consecutive elective CABG patients on self-report measures including optimism, illness representations, self-rated health, social support, coping methods, depression, anxiety and post-traumatic stress disorder. Poor pre-operative psychological functioning was the strongest psychological risk factor for adverse psychological functioning six months post-operatively [37].

## 5. Happiness

Negative emotional states (e.g., depression, anxiety) are proven risk factors for cardiovascular disease; however, much less is known about the association between positive emotional states (e.g., happiness and optimism) and cardiovascular health. Steptoe et al. have suggested that positive emotions may have direct and beneficial effects on physiological processes including those involving the neuroendocrine, inflammatory, immunological and cardiovascular systems [38]. The association between positive psychological well-being and mortality could be mediated in part via behavioural pathways. For example positive dispositions are related to predictors of prolonged survival, such as not smoking, exercising regularly, reduced alcohol consumption, and better sleep quality. Psychologically balanced persons might have increased adherence to medical regimens because inverse associations between adherence and depression have been described. However, the protective effect of positive emotions on mortality in healthy population studies persisted even after fully controlling for behavioural covariates, suggesting that other pathways may also be involved. Direct physiological pathways might also contribute to associations. Positive psychological well-being could alter people's disease susceptibility via the attenuation of sympathetic nervous system activity and the enhancement of parasympathetic activation. Positive affects may reduce stress-induced elevations of inflammatory and coagulation factors, such as fibrinogen and interleukin-6, which are crucial in cardiovascular disease, and reduce vulnerability to infectious illness. Positive psychological well-being was associated with reduced cardiovascular mortality in healthy population studies, with a near significant effect in patients with established cardiovascular disease [39]. In one of prospective epidemiological cohort studies participants with greater emotional vitality were at markedly reduced risk for CHD, and this effect remained significant after controlling for medical and psychosocial factors [40]. Optimism was associated with recovery from CABG surgery within 6 months [41]. Post hoc analysis of previous data showed that among depressed post-CABG patients, optimists responded to depression treatment at higher rates. Independent of depression, optimists were less likely to be rehospitalized by 8 months after CABG [42].

## 6. Illness intrusiveness

One of the important determinants of quality of life is taking part in psychologically meaningful activity. Illnesses, mostly chronic ones interfere with valued activities. Illness intrusive-

ness is a determinant of quality of life in patients with chronic disease. Illness intrusiveness covers the disease- and treatment-induced disruptions to lifestyles, activities, and interests [43]. There is only one available study about the relationship of illness intrusiveness and CABG: our work group investigated psychosocial factors like illness intrusiveness, depression, anxiety, sleeping disorders and found an independent association with the occurrence of major adverse cardiac and cerebrovascular events (MACCE) after adjustment of biomedical factors and perioperative variables following cardiac surgery. Additionally, severity of illness intrusiveness, sleeping problems and social inhibition increased in the MACCE positive patients during the three-year period; these tendencies were not observed in the event-free group [44].

## 7. Quality of life

With aging of the population and sophisticated health care technologies the number of patients with chronic diseases has extremely increased. As a result, improving the daily functioning and quality of life of the chronically ill has become an important goal of medical and surgical interventions. Therefore assessing the quality of life has been brought into the limelight [45]. On the other hand, predictive value of quality of life on survival and other outcomes of cardiac surgery has been also studied. In a prospective study of 6305 patients who underwent isolated coronary artery bypass the overall functional health-related quality of life improved after recovery from cardiac surgery. Reduced long-term survival following cardiac surgery even after adjustment for known risk factors associated with survival after cardiac surgery was associated with lower functional health related quality of life beyond the posthospital recovery phase. The degree of functional recovery was directly related to subsequent survival [46]. In a prospective cohort study the preoperative quality of life was an independent predictor of 6-month mortality following CABG even after adjusting for traditional risk factors. The magnitude of the effect (39% increase in risk for a small difference in quality of life score) was clinically important, and it is a non-invasive, easily available tool for clinicians [47].

## 8. Gender differences

The increased operative mortality and morbidity of women compared with men undergoing CABG surgery results from differences in methodology, low number of women in studies reporting negative findings, many studies, both positive and negative, did not take into account preoperative differences in health status between the sexes. Women more frequently have factors associated with increased short- and long-term mortality, such as less common use of internal mammary artery grafts. According to the reported analyses, they are older, less educated, have more severe angina and congestive heart failure, lower functional status, and higher level of depressive symptoms. At time of referral, women are at more advanced disease stage than men; however, despite being more symptomatic, women have less extensive coronary artery disease than men as determined by coronary angiography results [48]. This



large number of differences makes the comparison difficult, and studies are not corrected for so many potential imbalances that may influence sex differences in outcome. Additional large prospective studies with substantial numbers of women are needed to evaluate gender-related differences in autonomic responses to myocardial infarction, complications related to cardiopulmonary bypass, susceptibility to abnormalities in coagulation, and other biological factors that might account for discrepant outcomes in men versus women undergoing CABG. Furthermore, specific pharmacologic and therapeutic considerations, such as the role of estrogen replacement therapy, need to be clarified [49]. Compared to conducted studies in this topic the POST CABG Biobehavioral Study enrolled the highest number of women ( $n = 269$ ) and physical, social, and emotional functioning were investigated after CABG surgery. Both male and female patients improved in physical, social, and emotional functioning after CABG, and recovery over time was similar in men and women. However, women's health-related quality-of-life scale scores remained less favourable than men's women did show less benefit with regard to the symptoms of shortness of breath and tiredness through 1 year after surgery [50]. In another prospective cohort study on quality of life women did not reach the same degree of improvement after 1 year as men, even after adjusting for pre-existing risk factors. Women were at greater risk for subjective cognitive difficulties, increased anxiety and decreased ability to perform tasks for daily living, diminished work-related activities, and reduced exercise capacity [51].

## 9. Social support

Socially isolated persons are single and/or have small social network. Social isolation is associated with poor outcome in established CAD, while high levels of social support is known to promote psychologic and physical well being [52]. Social support can be divided into two broad categories: social networks, which describe the size, structure, and frequency of contact with the network of people surrounding an individual; and functional support, which may be further divided into received social support, which highlights the type and amount of resources provided by the social network, and perceived social support, which focuses on the subjective satisfaction with available support or the perception that support would be available if needed [2]. The underlying mechanisms remain to be identified. Several factors may confound the effect of isolation such as disease severity, or its associations with demographic measures, because socially isolated patients are generally older and of lower socioeconomic status, which are known to reduce survival. Another possible mechanism is the influence of disease progression via its effect on psychosocial functioning. Psychological distress in CAD patients is more severe in patients with lack of adequate social support. Description of the demographic and psychosocial characteristics of those with few social contacts might aid our understanding of the link between isolation and mortality [52]. Previous studies showed the pivotal role of family ties in preserving cardiovascular health [53, 54]. A strong and consistent inverse gradient was reported between the magnitude of social support and adverse clinical outcomes among both initially healthy subjects and those with known CAD [55]. In our study on cardiac surgery patients (180 patients) 17% of patients admitted living alone, however when

asking about marital status 35% admitted being single. We showed in our study that social isolation was associated with higher mortality after cardiac surgery [27]. Without social network and family support patients face longer hospital stay after CABG. Loneliness increases mortality: in a prospective study 1290 CABG patients were investigated. After controlling for various preoperative factors known to be independently associated with mortality loneliness was found to be associated with mortality, both at 30 days (relative risk 2.61) and at 5 years (relative risk 1.78) after the operation [52]. Kopp et al. found that marital status and spouse support was closely associated with men's mortality. Premature death was significantly lower among married men or men in relationship compared to single men and those who were satisfied with spouse support compared to those who were not [56]. Orth-Gomer et al. reported that following myocardial infarction, women with concomitant marital stress had 2.9-fold increased risk of recurrent cardiac events during a five-year follow-up compared to those with less marital stress after adjustment for age, estrogen status, education level, smoking, diagnosis at index event, diabetes mellitus, systolic blood pressure, smoking, triglyceride level, high-density lipoprotein cholesterol level, and left ventricular dysfunction [57]. In accordance with this finding, higher prevalence of subclinical atherosclerosis, and accelerated progression over time, among healthy women reporting marital dissatisfaction was reported, assuming that marital stress is atherogenic [58].

## 10. Negative affectivity and social inhibition

Type D personality unifies psychosocial factors related to high cardiovascular risk in one model. Particularly negative affectivity (NA) and social inhibition (SI) are relevant in this context. NA refers to the stable tendency to experience negative emotions across time/situations. Persons with high-NA experience more feelings of dysphoria, anxiety, and irritability; have a negative view of self; and are looking for signs of impending trouble. NA overlaps with neuroticism and trait anxiety; includes subjective feelings of tension, worry, anxiety, anger, and sadness. SI patients tend to inhibit the expression of emotions/behaviours in social interactions to avoid disapproval by others. They feel inhibited, tense, and insecure when with others. Individuals who are high in both NA and SI have a distressed or Type D personality, given their vulnerability to chronic distress [59]. Type D patients are at increased risk for a wide range of adverse health outcomes, mortality and morbidity, in various cardiovascular populations, including those with ischemic heart disease [60], coronary intervention [61], cardiac arrhythmias [62], peripheral arterial disease [63]. Global left ventricular dysfunction and type D personality were independent predictors of long-term cardiac events in patients with a reduced ejection fraction after myocardial infarction [64]. Type D personality independently predicted mortality and early allograft rejection after heart transplantation [65]. In our 5-year follow-up, there was no link between the occurrence of major cardiac and cerebral event and NA and SI after CABG [44]. Additionally, severity of illness intrusiveness, sleeping problems and SI increased in the MACCE positive patients during the three-year period. Unfavourable effect of Type D is linked to physiological hyperreactivity, immune activation, and inadequate response to cardiac treatment [59].

First author and title	Number of patients	Methods	Results
Cserép Z. Psychosocial factors and major adverse cardiac and cerebrovascular events after cardiac surgery.	180	Depression [Beck depression inventory (BDI)], anxiety [state anxiety subscale in Spielberger State-Trait Anxiety Inventory (STAI-S) and trait anxiety subscale in Spielberger State-Trait Anxiety Inventory (STAI-T)] were investigated annually, social support, negative affectivity, social inhibition (SI), illness intrusiveness, self-rated health and sleeping disorders were investigated by standardized tests at the second and fifth year after cardiac surgery. The end-point was the major adverse cardiac and cerebrovascular event (MACCE) including death.	At the end of the second year after adjustment for medical and perioperative factors worse self-rated health [adjusted hazard ratio (AHR): 0.67, P=0.006], sleeping disorders (AHR: 1.14, P=0.001), higher illness intrusiveness (AHR: 1.03, P=0.018), higher BDI (AHR: 1.12, P=0.001), STAI-S (AHR: 1.09, P=0.001) and higher STAI-T scores (AHR: 1.08, P=0.002) showed higher risk for MACCE. Significant individual elevation in scores of sleeping disorders, illness intrusiveness and SI were observed over the three-year period in the MACCE group.
Denollet J. Personality as independent predictor of long-term mortality in patients with coronary heart disease.	268 men and 35 women	Patients with angiographically documented CHD, who were taking part in an outpatient rehabilitation programme. All patients completed personality questionnaire at entry to the programme. Survival status was followed up for mean 7-9 years. The main endpoint was death from all causes.	The rate of death was higher for type-D patients than for those without type-D (23 [27%]/85 vs 15 [7%]/218; p < 0.00001). The association between type-D personality and mortality was still evident more than 5 years after the coronary event and was found in both men and women. Type-D was an independent predictor of both cardiac and non-cardiac mortality after controlling for medial variables.
Pedersen SS. Type D personality predicts death or myocardial infarction after bare metal stent or sirolimus-eluting stent implantation: a Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry sub-study.	875	Patients completed the Type D Personality Scale (DS14) six months after PCI. The end point was a composite of death and MI.	Type D patients were at a cumulative increased risk of adverse outcome compared with non-Type D patients: 5.6% versus 1.3% (p < 0.002). Type D personality (odds ratio [OR] 5.31; 95% confidence interval [CI] 2.06 to 13.66) remained an independent predictor of adverse outcome adjusting for all other variables.

Pedersen SS. Type D personality is associated with increased anxiety and depressive symptoms in patients with an implantable cardioverter defibrillator and their partners. 221	Patients with implantable cardioverter defibrillator and their partners completed the Hospital Anxiety and Depression Scale, the Type D Personality Scale, and the Perceived Social Support Scale.	In patients, Type D personality was independently related to anxiety (OR: 7.03; 95% CI: 2.32-21.32) and depressive symptoms (OR: 7.40; 95% CI: 2.49-21.94) adjusting for all other variables. In partners, Type D personality was independently associated with increased symptoms of anxiety (OR: 8.77; 95% CI: 3.19-24.14) and depression (OR: 4.40; 95% CI: 1.76-11.01).
Aquarius AE. Role of disease status and Type D personality in outcomes in patients with peripheral arterial disease. 150	Patients with peripheral arterial disease were assessed with the Type D Scale-14, World Health Organization Quality of Life Assessment Instrument-100, and Perceived Stress Scale-10 Item assessed type D personality, QOL, and perceived stress	Type D patients reported significantly poorer quality of life than non-type D patients across peripheral arterial disease and healthy subgroups ( $p < 0.0001$ ). After controlling for disease status (presence or absence of peripheral arterial disease), type D personality remained associated with increased risk for impaired quality of life (odds ratio [OR] 7.35, 95% confidence interval [CI] 3.39 to 15.96, $p < 0.0001$ ) and perceived stress (OR 6.45, 95% CI 3.42 to 12.18, $p < 0.0001$ ).
Denollet J. Personality, disease severity, and the risk of long-term cardiac events in patients with a decreased ejection fraction after myocardial infarction. 87	Patients with myocardial infarction with a decreased left ventricular ejection fraction (LVEF).	Patients with Type D personality were more likely to experience an event over time compared with non-type D patients ( $P=0.00005$ ). Cox proportional hazards analysis yielded LVEF of $< \text{or} = 30\%$ (relative risk, 3.0; 95% confidence interval, 1.2 to 7.7; $P=.02$ ) and type D (relative risk, 4.7; 95% confidence interval, 1.9 to 11.8; $P=0.001$ ) as independent predictors.
Denollet J. Unfavorable outcome of heart transplantation in recipients with type D personality. 51	Patients with transplanted heart were identified to have or not to have Type D personality by using the DS14 scale.	Type D recipients had a 10-fold higher mortality rate after hospital discharge (5 of 15, or 33%) as compared with non-Type D recipients (1 of 34, or 3%) ( $p = 0.013$ , adjusting for age and gender). Among surviving recipients, the rate of Grade $\geq 3A$ rejection for both groups was 40% vs 27%, respectively ( $p = 0.45$ ). The risk of unfavorable outcomes (death, Grade $\geq 3A$ rejection, or number rejection-free days $< \text{or} = 14$ ) was greater in Type D recipients (12 of 15, or 80%) than in

non-Type Ds (13 of 34, or 38%), adjusting for other risk factors (odds ratio: 6.75; 95% confidence interval: 1.47 to 30.97) ( $p = 0.014$ ).

**Table 3.** Some important studies about negative affectivity and social inhibition in cardiology

## 11. Education

Previous research showed that educational level is an important health determinant, with gender-related differences and ethnic and cultural variations. Low educated men and women, in particular with required schooling only, have usually low income and thus lower socio-economic status may be expected. The lower education level of older persons leads to greater burden for medical services and lower awareness of how to lead a healthy lifestyle, and lower adherence to medication and utilisation of preventive measures. In general, women take part more often in screening programs, are more interested in health prevention and visit their general practitioners more often. Their activity may also relate to a higher rate of diagnosis of depression and anxiety disorders. Besides biological factors including oestradiol, psychosocial factors, culture and education may be responsible for the prevalence of these mental disorders among women [66]. Less education was showed an important risk factor for late-life depression [67]. In survey in South America women's higher education was associated with lower risk for diabetes and hypertension and lower BMI in all areas but more strongly in urban areas. There was no association or even an adverse association between education and these risk factors among men in less urban areas [68]. Controversially, men with low level of education were related to higher BMI, prevalence of diabetes and smoking. Less-educated women had higher blood pressure and BMI and low education in both sexes was associated with twofold increased incidence of stroke and CHD [69]. In an Austrian study both men and women with lower educational levels were associated with unhealthy behaviours, overweight and higher cardiovascular risk. There was an inverse relationship in both men and women between overweight and obesity and educational level. The odds of daily smoking, eating a diet rich in meat and doing no regular vigorous exercise decreased with increasing educational level. Among women, the odds of suffering from diabetes or from hypertension decreased gradually with increasing educational level. There was no clear association between educational level and the risk of diabetes or hypertension in men. Depression among women with only required schooling was frequent, but showed no relationship with education in men [66]. Low education and income are important determinants of all-cause mortality and cardiovascular mortality [70] among patients with myocardial infarction. Low income and education are related to a higher risk profile and poorer treatment [71]. In accordance, in our study, a higher level of education was associated with a longer survival time after CABG. Those patients who had an academic degree had a mean survival time of 8.01 years, patients with 9 to 12 years of education had a mean survival time of 7.73 years and the group with 8 years or less of education had a mean survival time of 7.03 years. There were significant differences among patients with 8 years or less of education and patients with 8 to 12 years of education and patients with an



academic degree in the survival analysis. Patients with less education had a worse life expectancy. There was no significant difference between patients with 9 to 12 years of education and those with an academic degree [13]. Patients with a high level of education are likely to have a higher income and therefore can afford the more expensive “healthy” diet and sport activities [70]. In a recent study, however, the risk for major cardiac event after primary percutaneous coronary intervention depended only on employment status and income, but not education level [72]. More prospective studies are needed to establish the relationship.

## 12. Interventions

The American Heart Association has recommended routine screening by self-reporting measures to rapid identification of likely depressed CAD patients. The Patient Health Questionnaire is one such depression assessing measurement, focuses on two requisite symptoms for a depression or major depressive episode diagnosis, i.e., (1) little interest or pleasure in doing things, (2) feeling down, depressed, or hopeless. Patients with positive screening results should be evaluated by a professional qualified in the diagnosis and management of depression [5].

### 12.1. Antidepressants

There are currently several empirically validated treatments for depression. A national survey of cardiovascular physicians reported nearly 50% of respondents treat the symptoms of depression once identified in patients with CAD [73]. The Selective serotonin re-uptake inhibitors (SSRI) are currently considered the safest to use with CAD patients, in contrast to the tricyclics, which may have pro-arrhythmic and cardio-toxic effects. The SSRI have been hypothesized as safe among cardiac patients due to the serotonin transporter affinity and attenuation of platelet functioning. The SADHART trial compared the effects of sertraline and placebo for 24 weeks in major depressive patients with unstable angina or recent MI. The SSRI treatment did not adversely affect cardiac function and was considered to be safe for most patients [74]. However, in the ENRICHD trial, improvements in depression were rather modest. Patients with at least 1 prior episode of depression or more severe depression showed consistent improvement in depression relative to control, suggesting that treatment with SSRIs is a good option for this subset of depressed CAD patients. The ENRICHD trial also found that antidepressant treatment improved prognosis for myocardial infarction patients, they were at decreased risk for death and reinfarction compared with those who did not take antidepressants [75]. In a systematic review [76] only 2 studies had follow-up periods that were long enough to assess cardiac outcomes [76, 77]. None of them found evidence of an effect of depression treatment. Two studies reported that selective serotonin reuptake inhibitors did not affect cardiac function [74, 79]. Possible side effects of SSRIs for CABG surgery patients include increased bleeding, but have not been consistently supported [80]. One study suggested an increased long-term mortality and rehospitalization after CABG surgery attributable to SSRIs [81]. Another study indicated greater renal morbidity and ventilation times, but not greater mortality or bleeding risk [82]. In two recent systematic reviews of randomized, controlled trials in CAD patients both established SSRI vs. placebo there was no difference in



mortality and differential findings were reported on hospital readmissions. One found reduced odds [83], whereas another review did not when applying stringent criteria for properly randomized studies [84]. There is no trial about the role of anxiolytic drugs before or after CABG with or without concomitant depressive symptoms.

## 12.2. Psychosocial Interventions

Psychosocial interventions (psychotherapy, support, stress reduction) have been used as treatments for depression in CAD patients. The aim of these interventions is to reduce psychological distress, which in theory would ultimately improve clinical outcomes. Patients with depression often do not participate or complete cardiac rehabilitation programs after CABG and thus may form a barrier to improvements in cardiac functioning [85]. From another aspect, isolated patients may be difficult to enroll in interventions because they do feel that they have a problem. Without the experience of need, motivation to change may be low [86]. Numerous behavioural and psychological randomized controlled trial (RCT) interventions have been reported and cognitive behavioural therapy or collaborative care constitutes Class IIa evidence (i.e., it is reasonable to administer treatment, additional studies with focused objectives are needed) [85]. In one of RCT studies on brief, tailored cognitive behavioural therapy targeting preoperative depression and anxiety researchers found that intervention improved depressive and anxiety symptoms, as well as quality of life. Moreover, it reduced in-hospital length of stay [87]. In a Canadian study eight weeks prior to CABG, the treatment group received exercise training twice per week, education and reinforcement, and monthly nurse-initiated telephone calls. After surgery, participation in a cardiac rehabilitation program was offered to all patients. The intervention was not associated with differences in pre-surgery anxiety versus usual care, however length of stay differed significantly between groups. Patients who received the preoperative intervention spent 1 less day in the hospital overall and less time in the intensive care. During the waiting period, patients in the intervention group had a better quality of life than controls. Improved quality of life continued up to 6 months after surgery. Mortality rates did not differ [88]. In a prospective randomized controlled trial the effects of a home-based intervention program on anxiety and depression 6 months after CABG were assessed. Anxiety and depression symptoms were measured before surgery, 6 weeks after surgery, and 6 months after surgery. On 6-week and 6-month follow-ups, significant improvements in anxiety and depression symptoms were found in both groups. There was no significant difference between patients receiving interventions and not [89]. Freedland et al. compared cognitive behaviour or supportive stress management vs usual care and found significant three month depression remission rates in the treatment arms. Cognitive behaviour therapy had greater and more durable effects than supportive stress management on depression and several secondary psychological outcomes [90]. The limitation of psychosocial RCTs among CABG populations is that those patients experiencing significant post-operative morbidity are likely to be excluded from trial inclusion. Therefore, less is known about long term outcomes for patients who experience stroke, deep sternal wound infection, sternal dehiscence, renal failure requiring dialysis and extended length of time on mechanical ventilation, or intensive care during their hospital stay. These moribund patients are at higher risks for developing or exacerbating psychological distress. Moreover, treatment of affective

disorders is important in any context, there is not sufficient evidence whether interventions among cardiac patients can promote and maintain health related behaviour change [25]. Exercise is commonly recommended to promote both primary and secondary CAD prevention, but evidence suggests that exercise may also modify psychosocial risk factors, including depression. Cross sectional studies of both patients and healthy cohorts have consistently demonstrated lower depression rates among those who are most active [55]. A randomized controlled comparison between antidepressant medication versus exercise was performed in depressed patients. After 16 weeks, there was a significant reduction in depression in all groups, confirming the same effect of exercise and sertraline hydrochloride in reducing depressive symptoms. However, a lower rate of relapse was observed in the exercise group after six months [91].

### 13. Conclusion and future directions

Coronary artery bypass graft surgery (CABG) is a confirmed procedure to relieve angina pectoris and reduce the risk from life-threatening ischaemic heart disease, besides reducing the likelihood of future heart attacks and prolonging life-expectancy. Another goal is to improve health-related quality of life and psychological well-being. After successful surgery the majority of patients can have an improved everyday life, with increased performance in physical, social and sexual functioning and decreased levels of depression, anxiety, fatigue and sleep. In some cases quality of life for patients can be disappointing, and attention has increasingly been paid to psychological difficulties following CABG surgery [92]. Psychological problems such as depression and anxiety are widely reported soon after CABG surgery and remain evident for around one-fifth of patients one year after surgery. Poor psychological adjustment following surgery can increase the likelihood of new coronary events, further hospitalisations and even death. According to a recent study 30% of patients have reduced health related quality of life without being clinically anxious or depressed they present with fear of activity, fear of excitement, give up enjoyed hobbies / activities. Evidence suggests that self-perceived health related quality of life, depressive symptoms and anxiety together influence the short and long term recovery following coronary bypass surgery [93]. There is also a higher risk for morbidity and mortality among the lonely and the socially isolated, they are likely to have prolonged postoperative recovery and hospital stay. Lower education and poor social background are associated with higher mortality rates related to CHD and prolonged hospital stay after CABG [93, 94]. Further research on the interaction between these disorders and social factors may improve our understandings and uncover promising ways for intervention. Most studies to date focus on depression, the role of other factors alone or investigated together warrants further research.

In conclusion, compared with community samples the prevalence of depression and anxiety disorders are significantly higher and they confer greater morbidity risks, though the behavioural and biological mechanisms are poorly understood. Researchers and clinicians hope psychosocial intervention might decrease or cease the deleterious impact of depression and anxiety on morbidity and mortality.

## Author details

Zsuzsanna Cserép<sup>1</sup>, Andrea Székely<sup>1,2</sup> and Bela Merkely<sup>3</sup>

\*Address all correspondence to: szekelya@kardio.hu

1 Department of Anesthesiology and Intensive Care, Semmelweis University, Budapest, Hungary and Uzsoki Street Hospital of the Budapest Municipality, Budapest, Hungary

2 Intensive Care, Gottsegen György Hungarian Institute of Cardiology, Budapest, Hungary

3 Department of Cardiology, Semmelweis University, Budapest, Hungary

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